

Claims

1. A method of determining an angiotensin converting enzyme (ACE) genotype in a sample, comprising:

amplifying DNA from the sample with a first pair of flanking primers that hybridize to nucleic acid sequences flanking an ACE gene sequence, the presence of which indicates the presence of a first ACE gene variant, and the absence of which indicates the presence of a second ACE gene variant, and a third primer that specifically binds to said ACE gene sequence and together with one of the flanking primers forms a second pair of primers; and

detecting three nucleic acid products of the amplification, wherein the nucleic acid products indicate the ACE genotype in the sample.
2. The method of claim 1 wherein the amplification comprises performing a single polymerase chain reaction amplification.
3. The method of claim 1 wherein the sample is a human sample.
4. The method of claim 3 wherein the method distinguishes between genotypes selected from the group consisting of: insertion/insertion, insertion/deletion, deletion/deletion.
5. The method of claim 3 wherein the DNA is un-degraded DNA.
6. The method of claim 5 wherein the sample is a live tissue sample.
7. The method of claim 6 wherein the sample is selected from the group consisting of: blood, cultured cells, cells derived from amniotic fluid, and cells derived from chorionic villi.
8. The method of claim 1 wherein the live tissue sample is blood.

9. The method of claim 3 wherein the ACE sequence resides on Intron 16 of chromosome 17q23.
10. The method of claim 3 wherein the ACE sequence is a 287 base pair nonsense DNA domain.
11. The method of claim 3 wherein the first pair of flanking primers have the nucleic acid sequences 5'-CCA TCC TTT CTC CCA TTT CTC T-3' and 5'-GGA TGG TCT CGA TCT CCT GA-3'; and
the third primer has the nucleic acid sequence 5'-CCT TAG CTC ACC TCT GCT TGT AA-3'.
12. The method of claim 1 wherein the amplification comprises performing a single polymerase chain reaction amplification.
13. The method of claim 3 wherein the DNA sample is from a source selected from the group consisting of: the endothelium of blood vessels, epithelial cells, blood mononuclear cells, macrophages, male germinal cells, and a biological fluid.
14. The method of claim 3 wherein the nucleic acid products consist of a first nucleic acid fragment of approximately 123 base pairs, a second nucleic acid fragment of approximately 157 base pairs, and a third nucleic acid fragment of approximately 410 base pairs.
15. The method of claim 11 wherein the nucleic acid products consist of a first nucleic acid fragment of 123 base pairs, a second nucleic acid fragment of 157 base pairs, and a third nucleic acid fragment of 410 base pairs.
16. The method of claim 15 wherein:
when the first nucleic acid fragment is not present and the second and third nucleic acid fragments are present, the genotype is I/I;

when the first, second, and third nucleic acid fragments are present, the genotype is I/D;
and

when the first nucleic acid fragment is present and the second and third nucleic acid fragments are not present, the genotype is D/D.

17. A substantially pure nucleic acid sample comprising one or more nucleic acids selected from the group consisting of:

5'-CCA TCC TTT CTC CCA TTT CTC T-3'; 5'-GGA TGG TCT CGA TCT CCT GA-3'; and 5'-CCT TAG CTC ACC TCT GCT TGT AA-3'.

18. The substantially pure nucleic acid sample of claim 17 comprising each of:

5'-CCA TCC TTT CTC CCA TTT CTC T-3'; 5'-GGA TGG TCT CGA TCT CCT GA-3'; and 5'-CCT TAG CTC ACC TCT GCT TGT AA-3'.

19. A method of determining an angiotensin converting enzyme (ACE) genotype in a sample, comprising:

amplifying DNA from the sample with a first pair of flanking primers that hybridize to nucleic acid sequences flanking an ACE gene sequence, the presence of which indicates the presence of a first ACE gene variant, and the absence of which indicates the presence of a second ACE gene variant, and a third primer that specifically binds to said ACE gene sequence and together with one of the flanking primers forms a second pair of primers; and

detecting one or more nucleic acid products of the amplification, wherein the nucleic acid products indicate the ACE genotype in the sample;

wherein the first pair of flanking primers have the nucleic acid sequences 5'-CCA TCC TTT CTC CCA TTT CTC T-3' and 5'-GGA TGG TCT CGA TCT CCT GA-3'; and

the third primer has the nucleic acid sequence 5'-CCT TAG CTC ACC TCT GCT TGT AA-3'.

20. The method of claim 19 wherein the amplification comprises performing a single polymerase chain reaction amplification.

21. The method of claim 19 wherein the sample is a human sample.

22. The method of claim 21 wherein the method distinguishes between genotypes selected from the group consisting of: insertion/insertion, insertion/deletion, deletion/deletion.

23. The method of claim 21 wherein the ACE sequence resides on Intron 16 of chromosome 17q23.

24. The method of claim 21 wherein the ACE sequence is a 287 base pair nonsense DNA domain.

25. The method of claim 21 wherein the DNA sample is from a source selected from the group consisting of: the endothelium of blood vessels, epithelial cells, blood mononuclear cells, macrophages, male germinal cells, and a biological fluid.

26. The method of claim 21 wherein the nucleic acid products consist of a first nucleic acid fragment of 123 base pairs, a second nucleic acid fragment of 157 base pairs, and a third nucleic acid fragment of 410 base pairs.

27. The method of claim 26 wherein:

when the first nucleic acid fragment is not present and the second and third nucleic acid fragments are present, the genotype is I/I;

when the first, second, and third nucleic acid fragments are present, the genotype is I/D;

and

when the first nucleic acid fragment is present and the second and third nucleic acid fragments are not present, the genotype is D/D.

28. A kit for determining the genotype for angiotensin converting enzyme (ACE) in a sample comprising:

a primer comprising the nucleic acid sequence 5'-CCA TCC TTT CTC CCA TTT CTC T-3';

a primer comprising the nucleic acid sequence 5'-GGA TGG TCT CGA TCT CCT GA-3'; and

a primer comprising the nucleic acid sequence 5'-CCT TAG CTC ACC TCT GCT TGT AA-3';

in an amount sufficient to perform at least one polymerase chain reaction amplification of a nucleic acid sample; and

solvent and reagents adapted for determining the genotype for angiotensin converting enzyme (ACE) in a mammal.

29. A method for identifying a patient with a heightened risk of suffering from a disease comprising:

determining the angiotensin converting enzyme (ACE) genotype in a sample from the patient by amplifying DNA from the sample with a first pair of flanking primers that hybridize to nucleic acid sequences flanking an ACE gene sequence, the presence of which indicates the presence of a first ACE gene variant, and the absence of which indicates the presence of a second ACE gene variant, and a third primer that specifically binds to said ACE gene sequence and together with one of the flanking primers forms a second pair of primers; and detecting one or

more nucleic acid products of the amplification, wherein the nucleic acid products indicate the ACE genotype in the sample;

correlating the ACE genotype of the patient with a treatment regimen designed to treat or prevent one or more diseases selected from the group consisting of: myocardial infarction, ischemic and idiopathic dilated cardiomyopathy, sudden death in hypertrophic cardiomyopathy, coronary atherosclerosis, and restenosis after percutaneous transluminal coronary angioplasty.

30. The method of claim 29 wherein the treatment regimen is designed to treat myocardial infarction or coronary atherosclerosis.

31. The method of claim 29 wherein the method distinguishes between genotypes selected from the group consisting of: insertion/insertion, insertion/deletion, deletion/deletion.

32. The method of claim 29 wherein the genotype is determined by detecting the presence or absence of each of three nucleic acid products of the amplification reaction.

33. The method of claim 30 wherein the pair of flanking primers have the nucleic acid sequences 5'-CCA TCC TTT CTC CCA TTT CTC T-3' and 5'-GGA TGG TCT CGA TCT CCT GA-3'; and

the third primer has the nucleic acid sequence 5'-CCT TAG CTC ACC TCT GCT TGT AA-3'.

34. A method of determining a genotype for a gene of interest in a sample, comprising:

amplifying DNA from the sample with a first pair of flanking primers that hybridize to nucleic acid sequences flanking a sequence in said gene of interest, the presence of which indicates the presence of a first gene variant, and the absence of which indicates the presence of a

second gene variant, and a third primer that specifically binds to said gene sequence and together with one of the flanking primers forms a second pair of primers; and

detecting three nucleic acid products of the amplification, wherein the nucleic acid products indicate the genotype of the gene of interest in the sample.

35. The method of claim 34 wherein the amplification comprises performing a single polymerase chain reaction amplification.

36. The method of claim 34 wherein the sample is a human sample.

37. The method of claim 34 wherein the DNA sample is from a source selected from the group consisting of: the endothelium of blood vessels, epithelial cells, blood mononuclear cells, macrophages, male germinal cells, and a biological fluid.

38. The method of claim 34 wherein the nucleic acid products consist of a first nucleic acid fragment of approximately 123 base pairs, a second nucleic acid fragment of approximately 157 base pairs, and a third nucleic acid fragment of approximately 410 base pairs.

39. The method of claim 34 wherein the nucleic acid products consist of a first nucleic acid fragment of 123 base pairs, a second nucleic acid fragment of 157 base pairs, and a third nucleic acid fragment of 410 base pairs.